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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/775,840	01/31/2001	Brian P. Dwyer	257/245	2714

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EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/775,840	DWYER ET AL.	
	Examiner	Art Unit	
	MY-CHAU T TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41,44,49-52,54-57,59,60,62,64-66,71 and 114* is/are pending in the application.

4a) Of the above claim(s) *60* is/are withdrawn from consideration.

5)☒ Claim(s) *114* is/are allowed.

6)☒ Claim(s) *41,44,49-52,54-57,59,62,64-66 and 71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

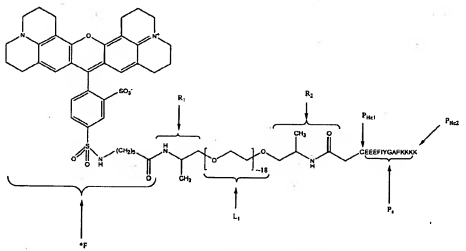
1. Applicant's amendment filed 11/04/2004 is acknowledged and entered. Claims 1-40, 42, 43, 45-48, 53, 58, 61, 63, 67-70, and 72-113 have been canceled. Claims 1, and 60 have been amended. Claim 114 has been added.

2. Claims 41, 44, 49-52, 54-57, 59, 60, 62, 64-66, 71, and 114 are pending.

Election/Restrictions

3. Applicant has elected the following species for the elected invention (Claims 41, 44, 49-52, 54-57, 59, 60, 62, 64-66, 71, and 114; drawn to a library of water-soluble pegylated kinase substrate):

a. The elected species of a library of water-soluble pegylated kinase substrate that would read on the formula of ***F-R_1-L_1-R_2-P_{Hc1}-P_S-P_{Hc2}-(R_3-L_2-R_4-T)$_y$** is



For the portion (R_3-L_2-R_4-T)$_y$, y = 0; therefore (R_3-L_2-R_4-T) is removed.

Note: the elected species is disclosed in the specification of page 34 (scheme 2), which is Texas Red-Jeffamine$_{900}$-CEEEFIYGAFKKKK [SEQ. ID. No. 1]. Furthermore, it is noted that "[F]or the portion $(R_3\text{-}L_2\text{-}R_4\text{-}T)_y$, y = 0; therefore $(R_3\text{-}L_2\text{-}R_4\text{-}T)$ is removed." P_{Hc1} is C (cysteine); therefore in the formula of $P_{Hc1} = A_c(A_H)_nA_m$, A_c = cysteine, A_m = covalent bond, and since n = 0 A_H is 0. P_{Hc2} is K (lysine); therefore in the formula of $P_{Hc2} = A_m(A_H)_nA_c$, A_c = carboxylic acid moieties since y = 0, A_m = covalent bond, and since n = 0, A_H is 0. P_s is EEEFIYGAFKKK (SEQ. ID. No. 1).

4. Claims 42, 43, 45-48, 58, 61, 63, 67-70, 72-77 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to ***nonelected species***, there being no allowable generic or linking claim. Election was made **without** traverse in Paper filed 3/12/04. Additionally, it is noted that claims 42, 43, 45-48, 58, 61, 63, 67-70, 72-77 have been canceled by the amendment filed 11/04/2004.

5. The amended claim 60 is directed to a ***nonelected species***. Claim 60 has added the limitation that "*y is not 0*". As claimed in claim 41, "*y is 0 or 1*", and thus the newly added limitation of claim 60 is interpreted to be y is 1. Additionally, the elected species of y is 0 and the election was made **without** traverse in Paper filed 3/12/04.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 60 is withdrawn from consideration as being directed to a non-elected species. See 37 CFR 1.142(b) and MPEP § 821.03.

6. Claims 41, 44, 49-52, 54-57, 59, 62, 64-66, 71, and 114 are treated on the merit in this Office Action.

Withdrawn Rejection(s)

7. The rejection of claims 41, 49-52, 54-57, 59, 60, and 71 under 35 USC 102(b) as being anticipated by Jacobs et al. (US Patent 5,853,723) has been withdrawn in light of applicant's amendment of claims 60.

8. The rejection of claims 41, 44, 49-52, 60, 64-66, and 71 under 35 USC 102(b) as being anticipated by Burbaum et al. (US Patent 5,876,946) has been withdrawn in light of applicant's amendment of claims 60. However, the rejections were rewritten in order to address the amendment of claim 60, wherein the amended of claim 60 is withdrawn from consideration as being directed to a nonelected species.

9. The rejection of claims 41, 44, 49-52, 54-57, 59, 60, 62, 64-66, and 71 under 35 USC 103(a) as being obvious over Jacobs et al. (US Patent 5,853,723) and Pomroy et al. (*Biochemical and Biophysical Research Communications*, **1998**, 245(2): 618-621) has been withdrawn in view of applicant's amendment of claim 60.

10. The rejection of claims 41, 49-52, 54-57, 59, 60, 62, 64-66, and 71 under 35 USC 103(a) as being obvious over Lam et al. (*Int. J. Peptide Protein Res.*, **1995**, 45(6): 587-592) and Jacobs et al. (US Patent 5,853,723) has been withdrawn in view of applicant's amendments of claim 60.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 41, 44, 49-52, 64-66, and 71 are rejected under 35 U.S.C. 102(b) as being anticipated by Burbaum et al. (US Patent 5,876,946).

Burbaum et al. disclose a library of peptidic substrates (see e.g. Abstract; col. 2, lines 55-63; col. 4, lines 31-48; col. 7, lines 45-48; col. 14, line 59 to col. 15, line 11). The peptidic substrate comprises a peptide (P_s) with a kinase domain affixed to a polymer bead and labeled with Cy5 (see e.g. col. 7, lines 45-48; col. 14, line 59 to col. 15, line 11) (refers to the presently claim "*F" of the formula; instant claims 49-51). The peptide comprises "end" residues with different net charged (see e.g. col. 14, lines 62-63) (refers to instant claims 64-66). The polymer bead includes polyethylene glycol (PEG)-grafted polystyrene bead (see e.g. col. 6, lines 44-61). The label includes other fluorescent label such as Texas red and chemiluminescent label (see e.g. col. 4, lines 31-41; col. 8, lines 62-65). The peptidic substrate of Burbaum et al. read on the claimed peptidic substrate member with the general formula of $*F\text{-}R_1\text{-}L_1\text{-}R_2\text{-}P_{Hc1}\text{-}P_S\text{-}P_{Hc2}\text{-}(R_3\text{-}L_2\text{-}R_4\text{-}T)_y$, wherein y is 0 (refers to claims 41 and 71), L_1 is polyethylene glycol (PEG) (refers to claims 41 and 52), R_1 is a covalent bond consisting of a nitrogen heteroatom (refers to claim 41), and R_2 is a covalent bond consisting of an oxygen heteroatom (refers to claim 41), P_{Hc1} is a lysine, i.e. in the formula of $P_{Hc1}= A_c(A_H)_nA_m$: A_c= lysine, A_m= covalent bond, and since n = 0, A_H is 0, and P_{Hc2} is a covalent bond with a carboxylic acid moiety, i.e. in the formula of $P_{Hc2}=$

$A_m(A_H)_nA_c$: A_c= carboxylic acid moieties since y = 0, A_m= covalent bond, and since n = 0, A_H is 0 (see e.g. col. 7, lines 45-48; col. 14, line 59 to col. 15, line 11). Thus the library of Burbaum et al. anticipates the presently claimed library.

13. Claims 41, 44, 49-51, 54-57 and 71 are rejected under 35 U.S.C. 102(b) as being anticipated by Belcheva et al. (*Polymeric Materials Science and Engineering*, **1998**, 79:471-472).

Belcheva et al. disclose the water-soluble fluorescein polymer-peptide conjugates (see e.g. pg. 471, left col., lines 12-25, and 35-39; pg. 472, lines 2-6; pg. 471, fig. 1; pg. 472, fig. 2; pg. 472, Table 1). The peptide (P_s) is 5 amino acids in length (see e.g. pg. 471, left col., lines 17-18, and 35-39; pg. 472, lines 2-6). The polymer is polyethylene glycol (PEG) with a MW of either 2000 or 5000 (see e.g. pg. 471, left col., lines 17-18, and 35-39; pg. 472, lines 2-6) (refers to instant claims 52, and 54-57). The water-soluble fluorescein polymer-peptide conjugates of Belcheva et al., i.e. GRGDY-PEG-fluorescein, read on the claimed substrate member with the general formula of $*F\text{-}R_1\text{-}L_1\text{-}R_2\text{-}P_{Hc1}\text{-}P_S\text{-}P_{Hc2}\text{-}(R_3\text{-}L_2\text{-}R_4\text{-}T)_y$, wherein y is 0 (refers to claims 41 and 71), *F is fluorescein (refers to instant claims 49-51), L_1 is polyethylene glycol (PEG), R_1 and R_2 are a covalent bond, P_{Hc1} is a covalent bond, i.e. in the formula of P_{Hc1}= $A_c(A_H)_nA_m$: A_c and A_m= covalent bond, and since n = 0, A_H is 0, and P_{Hc2} is a covalent bond with a carboxylic acid moiety, i.e. in the formula of P_{Hc2}= $A_m(A_H)_nA_c$: A_c= carboxylic acid moieties since y = 0, A_m= covalent bond, and since n = 0, A_H is 0 (see e.g. pg. 471, left col., lines 17-18, and 35-39; pg. 472, lines 2-6). Thus the water-soluble fluorescein polymer-peptide conjugates of Belcheva et al. anticipate the presently claimed library.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 41, 44, 49-52, 54-57, 59, 62, 64-66, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Belcheva et al. (*Polymeric Materials Science and Engineering*, **1998**, 79:471-472) and Pomroy et al. (*Biochemical and Biophysical Research Communications*, **1998**, 245(2): 618-621).

Belcheva et al. disclose the water-soluble fluorescein polymer-peptide conjugates (see e.g. pg. 471, left col., lines 12-25, and 35-39; pg. 472, lines 2-6; pg. 471, fig. 1; pg. 472, fig. 2; pg. 472, Table 1). The peptide (P_s) is 5 amino acids in length (see e.g. pg. 471, left col., lines 17-18, and 35-39; pg. 472, lines 2-6). The polymer is polyethylene glycol (PEG) with a MW of either 2000 or 5000 (see e.g. pg. 471, left col., lines 17-18, and 35-39; pg. 472, lines 2-6) (refers

to instant claims 52, and 54-57). The water-soluble fluorescein polymer-peptide conjugates of Belcheva et al., i.e. GRGDY-PEG-fluorescein, read on the claimed substrate member with the general formula of *F-R_1-L_1-R_2-P_{Hc1}-P_S-P_{Hc2}-(R_3-L_2-R_4-T)$_y$, wherein y is 0 (refers to claims 41 and 71), *F is fluorescein (refers to instant claims 49-51), L_1 is polyethylene glycol (PEG), R_1 and R_2 are a covalent bond, P_{Hc1} is a covalent bond, i.e. in the formula of P_{Hc1}= $A_c(A_H)_nA_m$: A_c and A_m= covalent bond, and since n = 0, A_H is 0, and P_{Hc2} is a covalent bond with a carboxylic acid moiety, i.e. in the formula of P_{Hc2}= $A_m(A_H)_nA_c$: A_c= carboxylic acid moieties since y = 0, A_m= covalent bond, and since n = 0, A_H is 0 (see e.g. pg. 471, left col., lines 17-18, and 35-39; pg. 472, lines 2-6).

The water-soluble fluorescein polymer-peptide conjugates of Belcheva et al. differ from the presently claimed invention by failing to include in the water-soluble fluorescein polymer-peptide conjugates a thioether linkage at R_2 position and the "end" residues (P_{Hc1} and P_{Hc2}) of the peptide has a different net charged.

Pomroy et al. disclose hydrophobic peptides wherein the peptide is coupled to the polyethylene glycol (PEG) by way of the cysteine with a PEG-a-cys reagent (Abstract; pg. 619, left col., line 60 to right col., line 2; fig. 2) (refers to claims 41, 44, and 59). The peptide comprises "end" residues (P_{Hc1} and P_{Hc2}) with different net charged (pg. 619, right col., lines 53-55) (refers to claims 64-66). There are several advantages for attaching Cys side chain to a thiol-reactive PEGs: 1) it can perform under mild reaction conditions allowing for the PEGylation of a target protein under non-denaturing conditions; 2) it is highly targeted; and the disulfide bond between the thiol-reactive Peg and the protein is cleavable with suitable disulfide-reducing agents (pg. 619, right col., lines 29-40).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include in the water-soluble fluorescein polymer-peptide conjugates a thioether linkage at R_2 position and the "end" residues (P_{Hc1} and P_{Hc2}) of the peptide has a different net charged as taught by Pomroy et al. in the library of Belcheva et al. One of ordinary skill in the art would have been motivated to include coupling the peptide to the polyethylene glycol (PEG) by way of the cysteine of the peptidic portion and the "end" residues (P_{Hc1} and P_{Hc2}) of the peptide has a different net charged in the water-soluble fluorescein polymer-peptide conjugates of Belcheva et al. for the advantage of providing a cleavable disulfide bond between the thiol-reactive PEG and the protein (Pomroy: pg. 619, right col., lines 37-40) since both Belcheva et al. and Pomroy et al. disclose composition wherein the peptide is coupled to the polyethylene glycol (Belcheva: pg. 471, left col., lines 12-25, and 35-39; Pomroy: pg. 618, right col., lines 18-33). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Belcheva et al. and Pomroy et al. because Pomroy et al. disclose the success of PEGylation of the peptide using PEG-a-Cys reagent (pg. 620, lines 5-32; fig. 2).

Response to Argument(s)

17. Applicant's argument directed to the rejection under 35 USC 102(b) as being anticipated by Burbaum et al. (US Patent 5,876,946) was considered but they are not persuasive for the following reasons.

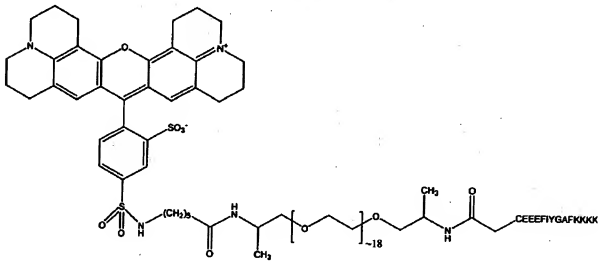
Applicant contends that the library of peptidic substrates Burbaum et al. does not anticipate the presently claimed invention because the recitation of the phrase "water-soluble"

has not been given patentable weight and thus the library of peptidic substrates of Burbaum et al. does not anticipate the presently claimed library.

In response to applicant's arguments, the recitation of the phrase "water-soluble" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Additionally, the library of peptidic substrates of Burbaum et al. meets all the structural limitations of the presently claimed library. That is the peptidic substrate of Burbaum et al. read on the claimed peptidic substrate member with the general formula of $*F\text{-}R_1\text{-}L_1\text{-}R_2\text{-}P_{Hc1}\text{-}P_S\text{-}P_{Hc2}\text{-}(R_3\text{-}L_2\text{-}R_4\text{-}T)_y$, wherein y is 0 (refers to claims 41 and 71), L_1 is polyethylene glycol (PEG) (refers to claims 41 and 52), R_1 is a covalent bond consisting of a nitrogen heteroatom (refers to claim 41), and R_2 is a covalent bond consisting of an oxygen heteroatom (refers to claim 41), P_{Hc1} is a lysine, i.e. in the formula of $P_{Hc1}= A_c(A_H)_nA_m$: A_c= lysine, A_m= covalent bond, and since n = 0, A_H is 0, and P_{Hc2} is a covalent bond with a carboxylic acid moiety, i.e. in the formula of $P_{Hc2}= A_m(A_H)_nA_c$: A_c= carboxylic acid moieties since y = 0, A_m= covalent bond, and since n = 0, A_H is 0 (see e.g. col. 7, lines 45-48; col. 14, line 59 to col. 15, line 11). Thus, the library of peptidic substrates of Burbaum et al. anticipates the presently claimed library, and the rejection is maintained.

Allowable Subject Matter

18. Claim 114 is allowable. The following is a statement of reasons for the indication of allowable subject matter: The cited prior art does not teach or fairly suggest the water-soluble peptidic substrate of claim 114 with the formula of



Conclusion

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
February 18, 2005

PADMASHRI PONNALURI
PRIMARY EXAMINER